Applicant(s): Kornowski et al. Application No.: 09/868,411

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In the claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please cancel claims 10, 11, 13, 28, 29, 45, 46, 58, 62, 63, 75, 79, 80, 91, 92 and 97-102 without prejudice.

Please amend claims 1-8, 12, 14-17, 19-27, 30-44, 47-53, 57, 59-61, 64-74, 76-78, 81-90 and 93-96 as follows:

- 1. (Currently Amended) A method of enhancing collateral blood vessel formation which comprises the step of in a subject comprising directly administering to a desired sites in heart or limb tissue a composition comprising an effective amount of autologous bone marrow aspirate to induce collateral blood vessel formation in the tissue.
- 2. (Currently Amended) The method of claim 1, wherein the autologous bone marrow aspirate is injected.
- 3. (Currently Amended) The method of claim 1, wherein the autologous bone marrow aspirate is injected intramyocardially.
- 4. (Currently Amended) The method of claim 3, wherein the autologous bone marrow aspirate is injected trans-epicardially or trans-endocardially.
- 5. (Currently Amended) The method of claim 4, wherein [[with]] the trans-endocardial approach is via a catheter-based approach is used.
- 6. (Currently Amended) The method of claim 1, wherein the autologous bone marrow aspirate is injected peripherally into the limb intramuscularly.

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7. (Currently Amended) The method of claim 1, wherein the autologous bone marrow

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aspirate has been stimulated ex vivo in culture.

8. (Currently Amended) The method of claim 7, wherein the autologous bone marrow

aspirate has been stimulated by contact with one or more angiogenesis stimulating cytokines or

other proteins or stimulating agents.

9. (Original) The method of claim 7, wherein the cytokines are selected from the group

consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

Claim 10. (Cancelled)

Claim 11. (Cancelled)

12. (Currently Amended) The method of claim 7, wherein the autologous bone marrow

aspirate has been stimulated ex vivo in culture by transient exposure to hypoxia or a form of

energy.

(Cancelled) Claim 13.

14. (Currently Amended) The method of claim 1, wherein the autologous bone marrow

aspirate is administered in combination with one or more agent selected from a

pharmacological drug, protein, or gene or any other compound or therapy that may enhance

that enhances bone marrow production of angiogenic growth factors and/or-selected to promote

endothelial cell proliferation, migration, or blood vessel formation.

15. (Currently Amended) The method of claim 14, wherein the autologous bone marrow

aspirate and the other agent or agents are administered together.

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16. (Currently Amended) The method of claim 14, wherein the autologous bone marrow

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aspirate and the other agent or agents are combined ex vivo prior to administration.

17. (Currently Amended) The method of claim 16, wherein the autologous bone marrow

aspirate has been stimulated ex vivo.

18. (Original) The method of claim 1, wherein ischemic tissue is treated.

19. (Currently Amended) A method of promoting the development of newly implanted

myocardial cells in a subject which comprises the step of directly administering an effective

amount of autologous bone marrow aspirate to the subject

20. (Currently Amended) The method of claim 19, wherein the autologous bone marrow

aspirate is injected.

21. (Currently Amended) The method of claim 19, wherein the autologous bone marrow

aspirate is injected intramyocardially.

22. (Currently Amended) The method of claim 21, wherein the autologous bone marrow

<u>aspirate</u> is injected trans-epicardially or trans-endocardially.

23. (Currently Amended) The method of claim 22, wherein with the trans-endocardial

approach is via a catheter-based approach is used.

24. (Currently Amended) The method of claim 19, wherein the autologous bone marrow

aspirate is injected peripherally into the limb intramuscularly.

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25. (Currently Amended) The method of claim 19, wherein the autologous bone marrow aspirate has been stimulated ex vivo.

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- 26. (Currently Amended) The method of claim 25, wherein the autologous bone marrow aspirate has been stimulated by <u>ex vivo</u> contact with one or more <u>angiogenesis stimulating</u> cytokines or other proteins or stimulating agents.
- 27. (Currently Amended) The method of claim [[25]] <u>26</u>, wherein the cytokines are selected from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

Claim 28. (Cancelled)

Claim 29. (Cancelled)

- 30. (Currently Amended) The method of claim 25, wherein the autologous bone marrow aspirate has been stimulated ex vivo by transient exposure to hypoxia or a form of energy.
- 31. (Currently Amended) The method of claim 25, wherein conditioned medium derived from the autologous bone marrow aspirate growing in culture is injected into [[the]] ischemic heart or limb.
- 32. (Currently Amended) The method of claim 19, wherein the autologous bone marrow is administered in combination with one or more agent selected from a pharmacological drug, protein, or gene or any other compound or therapy that may enhance bone marrow production of angiogenic growth factors [[and/or]] selected to promote endothelial cell proliferation, migration, or blood vessel formation.
- 33. (Currently Amended) The method of claim 32, wherein the autologous bone marrow aspirate and the other agent or agents are administered together.

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34. (Currently Amended) The method of claim 32, wherein the autologous bone marrow aspirate and the other agent or agents are combined prior to administration.

35. (Currently Amended) The method of claim 34, wherein the autologous bone marrow has been stimulated ex vivo.

36. (Currently Amended) A method of improving the electrical conductivity of the heart of a patient with cardiac electrical pathway impairment, which comprises the step of administering an effective amount of autologous bone marrow aspirate to the patient.

37. (Currently Amended) The method of claim 36, wherein the autologous bone marrow aspirate is injected.

38. (Currently Amended) The method of claim 36, wherein the autologous bone marrow aspirate is injected intramyocardially.

- 39. (Currently Amended) The method of claim 38, wherein the autologous bone marrow aspirate is injected trans-epicardially or trans-endocardially.
- 40. (Currently Amended) The method of claim 39, wherein [[with]] the trans-endocardial approach is via a catheter-based approach is used.
- 41. (Currently Amended) The method of claim [[36]][39, wherein [[with]] using the transendocardial approach the autologous bone marrow aspirate is injected peripherally into the limb intramuscularly.
- 42. (Currently Amended) The method of claim 36, wherein the autologous bone marrow aspirate has been stimulated ex vivo.

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43. (Currently Amended) The method of claim 42, wherein the autologous bone marrow

has been stimulated by contact ex vivo with one or more angiogenesis stimulating cytokines or

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other proteins or stimulating agents.

44. (Currently Amended) The method of claim [[42]]43, wherein the cytokines are selected

from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

Claim 45. (Cancelled)

Claim 46. (Cancelled)

47. (Currently Amended) The method of claim 42, wherein the autologous bone marrow

aspirate has been stimulated ex vivo by transient exposure to hypoxia or a form of energy.

48. (Currently Amended) The method of claim 42, wherein conditioned medium derived

from the autologous bone marrow growing in culture is injected into [[the]] ischemic heart

muscle [[or limb]].

49. (Currently Amended) The method of claim 36, wherein the autologous bone marrow is

administered in combination with one or more agents selected from a pharmacological drug,

protein, or gene or any other compound or therapy that may selected to enhance bone marrow

production of angiogenic growth factors and/or promote endothelial cell proliferation,

migration, or blood vessel formation.

50. (Currently Amended) The method of claim 49, wherein the autologous bone marrow

and the other agent or agents are administered together.

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51. (Currently Amended) The method of claim 49, wherein the autologous bone marrow

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and the other agent or agents are combined ex vivo prior to administration.

52. (Currently Amended) The method of claim 51, wherein the autologous bone marrow

has been stimulated ex vivo.

53. (Currently Amended) A method of enhancing myocardial function in a patient with

impaired myocardial function, which comprises the step of administering an effective amount

of autologous bone marrow to the patient.

54. (Original) The method of claim 53, wherein the autologous bone marrow is injected.

55. (Original) The method of claim 53, wherein the autologous bone marrow is injected

intramyocardially.

56. (Original) The method of claim 55, wherein the autologous bone marrow is injected

trans-epicardially or trans-endocardially.

57. (Currently Amended) The method of claim 56, wherein [[with]] the trans-endocardial

approach is via a catheter-based approach is used.

Claim 58. (Cancelled)

59. (Currently Amended) The method of claim 53, wherein the autologous bone marrow

has been stimulated ex vivo.

0. (Currently Amended) The method of claim 59, wherein the autologous bone marrow

has been stimulated by contact with one or more angiogenesis stimulating cytokines or other

proteins or stimulating agents.

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61. (Currently Amended) The method of claim 59, wherein the cytokines are selected from

the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

Claim 62. (Cancelled)

Claim 63. (Cancelled)

64. (Currently Amended) The method of claim 59, wherein the autologous bone marrow

aspirate has been stimulated by transient exposure to hypoxia or a form of energy.

65. (Currently Amended) The method of claim 59, wherein conditioned medium derived

from the autologous bone marrow aspirate growing in culture is injected into [[the]] ischemic

heart tissue or limb.

66. (Currently Amended) The method of claim 53, wherein the autologous bone marrow

aspirate is administered in combination with one or more agent selected from a

pharmacological drug, protein, or gene or any other compound or therapy that may selected to

enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell

proliferation, migration, or blood vessel formation.

67. (Currently Amended) The method of claim 66, wherein the autologous bone marrow

aspirate and the other agent or agents are administered together.

68. (Currently Amended) The method of claim 66, wherein the autologous bone marrow

aspirate and the other agent or agents are combined prior to administration.

69. (Currently Amended) The method of claim 68, wherein the autologous bone marrow

aspirate has been stimulated ex vivo.

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70. (Currently Amended) A method of treating an atrial or ventricular condition in the heart

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of a patient, which comprises the step of administering an effective amount of autologous bone

marrow aspirate to the patient.

71. (Currently Amended) The method of claim 70, wherein the autologous bone marrow

aspirate is injected.

72. (Currently Amended) The method of claim 70, wherein the autologous bone marrow

aspirate is injected intramyocardially.

73. (Currently Amended) The method of claim 72, wherein the autologous bone marrow

aspirate is injected trans-epicardially or trans-endocardially.

74. (Currently Amended) The method of claim 73, wherein [[with]] the trans-endocardial

approach is via a catheter-based approach is used.

Claim 75. (Cancelled)

76. (Currently Amended) The method of claim 70, wherein the autologous bone marrow

aspirate has been stimulated ex vivo.

77. (Currently Amended) The method of claim 76, wherein the autologous bone marrow

aspirate has been stimulated by contact with one or more angiogenesis stimulating cytokines. or

other proteins or stimulating agents.

78. (Currently Amended) The method of claim [[76]] 77, wherein the cytokines are selected

from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

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Claim 79. (Cancelled)

Claim 80. (Cancelled)

81. (Currently Amended) The method of claim 76, wherein the autologous bone marrow aspirate has been stimulated ex vivo by transient exposure to hypoxia or a form of energy.

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- 82. (Currently Amended) The method of claim 76, wherein conditioned medium derived from the autologous bone marrow aspirate growing in culture is injected into [[the]] ischemic heart tissue or limb.
- 83. (Currently Amended) The method of claim 70, wherein the autologous bone marrow aspirate is administered in combination with an agent selected from a pharmacological drug, protein, or gene or any other compound or therapy that may selected to enhance bone marrow production of angiogenic growth factors and/or promote endothelial cell proliferation or migration, or blood vessel formation.
- 84. (Currently Amended) The method of claim 83, wherein the autologous bone marrow aspirate and the other agent or agents are administered together.
- 85. (Currently Amended) The method of claim [[83]] <u>84</u>, wherein the autologous bone marrow <u>aspirate</u> and the <u>other</u> agent or agents are combined prior to administration.
- 86. (Currently Amended) The method of claim 85, wherein the autologous bone marrow aspirate has been stimulated.
- 87. (Currently Amended) A composition for the treatment of a cardiac or myocardial condition, which comprises an effective amount of <u>cultured</u> autologous bone marrow aspirate, wherein the cardiac or myocardial condition is treated.

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88. (Currently Amended) The composition of claim 87, wherein the autologous bone marrow aspirate has been stimulated ex vivo.

89. (Currently Amended) The composition of claim 88, wherein the autologous bone

marrow aspirate has been stimulated by contact with one or more angiogenesis stimulating

cytokines or other proteins or stimulating agents.

90. (Currently Amended) The composition of claim 89, wherein the cytokines are selected

from the group consisting of HIF-1, EPAS1, MCP-1, and CM-CSF.

Claim 91. (Cancelled)

Claim 92. (Cancelled)

93. (Currently Amended) The composition of claim 89, wherein the autologous bone

marrow aspirate has been stimulated by exposure to hypoxia.

94. (Currently Amended) The composition of claim 89, wherein further comprising

conditioned medium derived from the autologous bone marrow growing in culture is injected

into the ischemic heart or limb.

95. (Currently Amended) The composition of claim 87, wherein the autologous bone

marrow is administered in combination with further comprising a pharmacological drug,

protein, or gene or any other compound or therapy that may selected to enhance bone marrow

production of angiogenic growth factors and/or promote endothelial cell proliferation,

migration, or blood vessel formation.

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96. (Currently Amended) The composition of claim 87 which <u>further</u> comprises heparin or another anticoagulant.

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Claims 97-102. (Cancelled)